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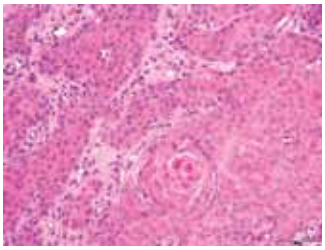
Research Briefs

Improving treatment options for feline squamous cell carcinoma

Using polyamines and combination therapy to inhibit cell growth



Dr. John Lewis, assistant professor of Dentistry and Oral Surgery, Department of Clinical Studies in Philadelphia and associate director of Mari Lowe Center for Comparative Oncology, first felt the frustration of dealing with feline oral squamous cell carcinoma (SCC) while on staff at a small animal practice in North Carolina. Although surgery can be curative in some cases, cats rarely show symptoms until the cancer has advanced to an inoperable size. In addition, oral SCC has historically been minimally responsive to radiation therapy and current chemotherapy options. When the opportunity arose, Dr. Lewis jumped at the chance to join a residency program at Penn Vet to further explore surgical and non-surgical options for improving the outcome for SCC patients.

SCC is the most common feline oral tumor, representing 70 percent of feline oral tumors. Since the median survival time from diagnosis to death or euthanasia is approximately 60 days, there is much room for improvement in treatment modalities. Dr. Lewis saw an opportunity to improve treatment options for patients who were not surgical candidates. In conjunction with Dr. Tom O'Brien's group at Lankenau Institute for Medical Research, Dr. Lewis and colleagues in Penn Vet's Oncology Section and Dentistry and Oral Surgery Service embarked on a Phase I/II clinical trial of polyamine inhibitor therapy for cats with spontaneously occurring oral SCC.

Polyamines are ubiquitous amino acid derived compounds that have been widely implicated in the growth and development of many mammalian tissues. When cellular polyamine synthesis is inhibited, cell growth is stopped or severely retarded. Providing exogenous polyamines restores the growth of cells. Polyamine synthesis is increased in many types of cancers and expression levels of the rate limiting synthetic enzyme, ornithine decarboxylase (ODC), are often increased as well. As Dr. O'Brien's original studies indicated that the ODC inhibitor difluoromethylornithine (DFMO) was effective in treating experimentally induced SCC in mice, a Phase I/II study was carried out to determine whether cats tolerate DFMO. Results of this study will soon be submitted for publication, but the relatively minimal side effects seen with DFMO protocols suggest that further studies are justified for use in a clinical setting.

Although targeting polyamine synthesis with ODC inhibitors can be effective for cancer cell growth inhibition, most eukaryotic cells have a polyamine transport system in their cell membrane that facilitates internalization of extracellular polyamines. Thus, polyamine synthesis inhibitors will only fight half the battle in reducing intracellular polyamine levels. To overcome this limitation, Dr. Lewis' latest study focuses on treating cats affected by oral SCC with a combination therapy utilizing DFMO and a polyamine transport inhibitor developed by MBF Therapeutics. The Veterinary Clinical Investigation Center (VCIC) has greatly facilitated all phases of this second study, and Dr. Lewis further credits the team effort put forth between Dr. Karin Sorenmo, Dr. Erika Krick, Dr. Nicola Mason, members of the Dentistry and Oral Surgery Service, Sections of Radiology and Pathology and practitioners who have shown interest in referring cases. While this study is still ongoing, it is the hope that such combined therapy will halt cancer growth but not significantly diminish other important quality of life aspects.

While increased research on feline oral SCC will undoubtedly benefit feline patients, it is Dr. Lewis' hope that such research will also have important implications for human patients.

CALL FOR NOMINATIONS

ALUMNI AWARDS of MERIT

The Executive Board of the Veterinary Medical Alumni Society is seeking nominations for the 2010 Alumni Award of Merit and other awards for distinguished Penn Vet Alumni. Alumni include matriculating graduates, as well as interns, residents and post-doctoral fellows.

To be presented at the Penn Annual Conference in March, 2011, these awards are given to alumni stars who have made outstanding contributions to their profession and to the School, through their contributions that advance knowledge in biomedicine, promote the welfare of animals through public education of animal owners and benefit society through civic activities that foster the advancement of the profession and the School's good name.

The Veterinary Medical Alumni Society Board is seeking any and all candidates, but specifically from 2010 reunion classes – or classes ending in '5 or '10.

Please forward your anonymous or signed nominations to Coreen M. Haggerty, Director of Alumni Relations, at 215.898.1481 or haggertc@vet.upenn.edu.